

## Reviewer's report

**Title:** Establishing normal ranges for fetal electrocardiogram values for the healthy fetus of 18-22 weeks of gestation: a prospective cohort study

**Version:2****Date:**24 November 2015

**Reviewer:**Jiri Spilka

### Reviewer's report:

Review:

Paper by Kim M.J. Verdurmen et al. Establishing normal ranges for fetal electrocardiogram values for the healthy fetus of 18-22 weeks of gestation: a prospective cohort study

Authors describe a prospective study with aim to determine normal values in fetal ECG (amplitudes and important intervals) in healthy fetuses during gestation (18-22 weeks).

The protocol for study is clearly written and very well presented.

The results of the proposed study will be useful in the field as fetal ECG characteristics from 18-22 weeks are not known.

Major comments:

- 1) The authors often use term "normal range" but this is never defined. What does normal range stands for? mean +/- std or mean (95% confidence intervals)?
- 2) It is not clear if the authors aim to determine normal ranges by per-week basis, i.e for 18, 19, ....., 23, 24 separately or if they are planning to group these weeks and consider it as one category? Natural approach is to consider these weeks separately as during weeks 18-24 there will be changes in fetal ECG as fetal heart grows and mature. This is discussed at P9L214-L217 for P-wave and QRS complex.
- 3) Calculation of required sample size is not clear. The value of 200 cases is stated but never explained.

Regarding my previous comments, is 200 cases enough for per-week analysis?

- 4) Authors also need to consider: i) loss of some patients, ii) bad quality of some records and inability to determine e.g. P-wave.

This needs to be discussed and taken into account for the required sample size.

- 5) More information should be given about fetal ECG device and about algorithm for semi-automatic analysis. As no automatic algorithm is 100% reliable

I would consider to involve experienced cardiologist to verify the automatic analysis. This would make the results of study more reliable.

- 6) There is no need to complicate the study by anomaly ultrasound examination by multiple sonographer. The final and correct identification of CHD will be performed postpartum. This would mean ex-post exclusion of only 2-3 cases since the prevalence of CHD is only 6-12/1000.
- 7) I do not understand the normalization procedure using vectorcardiogram.

Minor comments:

- I suggest to delete the word "Establishing" in the paper title. Thus title would read: Normal ranges for fetal electrocardiogram .....
- Specify for how long ECG will be recorded?
- Please be consistent with active/passive voice throughout the paper
- Authors will need informed consent from women
- P5L86-92 - Authors discuss new ultrasound methods such 3D and 4D and how these aid sonographer to visualize heart anatomy. Having better visualization of anatomy

I would expect also discussion how these methods help to reduce inter and intra observer variability in identification of CHD?

- P9L199: What is heart rate irregularity and how it is computed
- P9L208: quote: "defined as a % of interpolated data". What data are interpolated and when?
- P10L230: quote: "the fetal ECG is evaluated by semi-computerized algorithms, taking away the performer-dependent variability" this is not true.

As it is semi-automatic some observer variability will still be present.

Minor issues: Awkward phrases, typographical errors, suggestions:

P2L28: "65 to 81 per cent" -> 65 to 81%?

P2L29: "making this" -> making it

Abstract: passive vs active voice

P2L40: Awkward phrase: "Directly following, the fetal electrocardiogram will be conducted through dedicated signal processing methods"

P4L59,60,62: During pregnancy, during the course of pregnancy, during this examination -- consider rephrase and simplify

P4L61: "will be" -> are

P4L61: "will be" -> is

P5L106: delete "of the signal"

P5L110: "fetal hear rate: this is" -> fetal heart rate, which is

P8L179: Figure 2 provides no additional value to readers.